Correspondence

Internationally Recognized Antimicrobial Susceptibility Testing Methods and Interpretive Criteria: The Case for Conformity

To the Editor—The article by Helms et al. [1] raises a fundamental issue on the use of antimicrobial susceptibility testing, one that is crucial to the entire study. Bacterial isolates from patients are usually tested in clinical microbiology laboratories that use internationally recognized antimicrobial susceptibility testing methods, such as those of the Clinical and Laboratory Standards Institute (CLSI; formerly known as the NCCLS) or the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (available at: http://www.clsi.org and http://www.eucast.org). These organizations have experts who have established guidelines for appropriate antimicrobial susceptibility testing methods, quality control parameters for specific antibiotics and reference strains, and interpretive criteria that relate to clinical treatment outcomes. Use of these methods and criteria assures that testing is performed and results are interpreted appropriately. When another method is used and results are interpreted by other means, questions arise about the relationship of that method to the internationally recognized standard. In the case of the study by Helms et al., neither the CLSI nor the EUCAST antimicrobial susceptibility testing method was used. The result is that the classification of their clinical isolates as resistant was not fundamentally substantiated, thereby leading to questions about the relevance of their subsequent clinical analyses.

Specifically, the key issue is that a company-specific antimicrobial susceptibility testing method was used to classify an isolate as resistant. Susceptibility testing was performed by the tablet diffusion method with Neo-Sensitabs (Rosco). This method differs from the globally recognized CLSI disk diffusion method [2] in several important ways. First, the tablets contain higher concentrations of drug than do the standard paper disks used in CLSI tests, resulting in larger zones of growth inhibition and making comparisons between the methods problematic. Second, quality control parameters for antibiotics are developed in a defined multilaboratory study and established by consensus of the CLSI subcommittee on antimicrobial susceptibility testing; however, these cannot be applied to the tablet diffusion test. Third, the CLSI subcommittee establishes interpretive criteria for classification of isolates as susceptible, intermediate, or resistant by evaluation of clinical outcome data, pharmacokinetic/pharmacodynamic data, and scattergram (MIC:zone) data [3].

Campylobacter susceptibility testing has only recently been standardized by the CLSI. To date, only agar dilution and broth dilution have had methods and quality control parameters established [4, 5]. Disk diffusion methods remain problematic; thus, neither a standardized method nor quality control parameters have been established by the CLSI. Illustrating this point, a comparison of the E-test (which relies on drug diffusion into the agar) and the agar dilution reference method showed noncongruent outcomes for some antibiotics, in particular for nalidixic acid [6]. Thus, the use of disk and, by extension, tablet diffusion testing has not been validated for campylobacter.

In the study by Helms et al., the Neo-Sensitab tablet diffusion method was used to determine resistance to erythromycin and nalidixic acid. The authors used a zone-of-inhibition diameter of <27 mm as their interpretive criterion for resistance. However, the Neo-Sensitab product information brochure [7] states that the manufacturer's interpretive criteria for campylobacter resistance are actually <18 mm for nalidixic acid and ≤20 mm for erythromycin. This unexplained discrepancy in the authors' choice of using a zone size larger than that of the manufacturer would likely lead to more isolates being classified as resistant. Thus, there is the distinct possibility that isolates classified as resistant to either of the 2 antibiotics may, in fact, not be resistant.

Finally, there are no CLSI interpretive criteria available for any antibiotics used to treat campylobacteriosis. For convenience, classification of campylobacter isolates as susceptible, intermediate, or resistant is sometimes based on breakpoints established for Enterobacteriaceae. However, there is no medical or microbiological evidence that validates this extrapolation. The brochure for Neo-Sensitabs shows a regression analysis comparing zone-of-inhibition diameters that demonstrates that it is mathematically possible to extrapolate a MIC. However, this company-specific evaluation does not appear to have been established on the basis of clinical data; thus, it is of uncertain value. Regardless of the classification of isolates as resistant or not, Helms et al. should have confirmed the in vitro disk diffusion results via standardized dilution testing, to verify that the isolates classified as resistant did indeed have MICs higher than those that were classified as susceptible.

The use of internationally recognized susceptibility testing methods and interpretive criteria are essential for determining whether an isolate should be classified as resistant. In the case of the study by Helms et al., because the underlying classification of some campylobacter isolates as resistant to erythromycin and/or nali-

dixic acid is open to question for technical reasons, it follows that the subsequent clinical analyses in the study should be viewed with caution.

Thomas R. Shryock
Elanco Animal Health, Greenfield, Indiana

References

1. Helms M, Simonsen J, Olsen KEP, Mølbak K. Adverse health events associated with antimicrobial drug resistance in *Campylobacter* species: a registry-based cohort study. J Infect Dis **2005**; 191:1050–5.
2. NCCLS. Performance standards for antimicrobial disk susceptibility tests: approved standard [M2-A8]. 8th ed. Wayne, PA: NCCLS, **2003**.
3. NCCLS. Development of in vitro susceptibility testing criteria and quality control parameters: approved guideline [M23-A2]. 2nd ed. Wayne, PA: NCCLS, **2001**.
4. NCCLS. Performance standards for antimicrobial susceptibility testing: 14th informational supplement [M100-S14]. Wayne, PA: NCCLS, **2004**.
5. McDermott PF, Bodeis SM, Aarestrup FM, et al. Development of a standardized susceptibility test for *Campylobacter* with quality-control ranges for ciprofloxacin, doxycycline, erythromycin, gentamicin, and meropenem. Microbial Drug Resistance **2004**; 10:124–31.
6. Ge B, Bodeis S, Walker RD, et al. Comparison of the E-test and agar dilution for in vitro antimicrobial susceptibility testing of *Campylobacter*. J Antimicrob Chemother **2002**; 50:487–94.
7. Rosco Diagnostica A/S. Neo-Sensitabs™ User's Guide. 17th ed. **2004**. Available at: http://www.rosco.dk/Default.asp?ID=198. Last accessed 27 October 2005.

Potential conflict of interest: the author is employed by Elanco Animal Health, a division of Eli Lilly and Company.

Reprints or correspondence: Dr. Thomas R. Shryock, Elanco Animal Health, 2001 W. Main St., GL52, PO Box 708, Greenfield, IN 46140 (thomas.r.shryock73@lilly.com).

The Journal of Infectious Diseases 2005; 192:2027–8
 0022-1899/2005/19211-0024$15.00

Reply to Shryock

To the Editor—Quinolones stop bacterial cell growth by inhibiting DNA replication and transcription through alterations in DNA gyrase and topoisomerase IV, reduction of permeability, or expression of efflux pumps. Quinolone resistance in *Campylobacter jejuni* and *C. coli* arises most often through single-point chromosomal mutations in the *gyrA* gene, which encodes DNA gyrase [1–3]. A single-point chromosomal mutation, often found at aa 86 (threonine) in the *gyrA* gene, results in high-level resistance to nalidixic acid (MIC, 64–128 μg/mL) and ciprofloxacin (MIC, 16–64 μg/mL). This means that, in most situations, it is easy to phenotypically distinguish between quinolone-resistant and quinolone-susceptible *C. jejuni* and *C. coli* isolates on the basis of zone diameters, because resistant and susceptible isolates represent 2 distinct populations of bacteria. The <27-mm breakpoint for quinolone resistance was established by the Danish Integrated Antimicrobial Resistance and Monitoring and Research Programme (DANMAP) in 2000 [4]. This was several years before the Clinical and Laboratory Standards Institute (CLSI; formerly known as the NCCLS) established breakpoints for campylobacter and Rosco published its CLSI <18-mm breakpoint for nalidixic acid for use with Neo-Sensitabs [5, 6]. To check whether this difference in breakpoint would modify our results, we reanalyzed our data with the CLSI <18-mm breakpoint for nalidixic acid. A total of 90 (2.6%) of the 3471 isolates in our study had a zone diameter between 18 and 26 mm and were reclassified as quinolone susceptible according to the CLSI breakpoint, including 2 isolates from patients with adverse health events. According to Rosco's recommendation, isolates with a zone diameter <16 mm should be classified as resistant, and isolates with a zone diameter ⩾18 mm should be classified as susceptible. In this analysis, 12 and 9 strains with a zone diameter of 16 and 17 mm, respectively, were classified as re-

Table 1. No. of cases of invasive illness or death among 3471 patients with *Campylobacter* infection and odds ratios (ORs) for invasive illness or death within 30 and 90 days of the date of receipt of samples, according to resistance profile—Denmark, 1996–2000.

	0–30 days			0–90 days		
Profile	No. of adverse events[a]/ no. alive	OR (95% CI) Crude	OR (95% CI) Adjusted[b]	No. of adverse events[a]/ no. alive	OR (95% CI) Crude	OR (95% CI) Adjusted[b]
Resistant to						
Quinolone only	4/678	3.98 (1.15–13.78)	4.48 (1.23–16.30)	4/678	1.98 (0.68–5.83)	2.70 (0.85–8.54)
Erythromycin only	2/65	17.01 (3.24–89.32)	6.08 (0.67–55.48)	4/65	22.26 (7.38–67.11)	8.60 (1.86–39.77)
Quinolone and erythromycin	1/43	12.75 (1.46–111.5)	3.24 (0.22–48.63)	3/43	13.03 (2.77–61.34)	1.87 (0.22–15.92)
Susceptible to quinolone and erythromycin	4/2685	1.00	1.00	9/2685	1.00	1.00
Total	11/3471			20/3471		

NOTE. Breakpoints for resistance were <18 mm for nalidixic acid and ⩽20 mm for erythromycin. CI, confidence interval.
[a] Cases of invasive illness or death.
[b] Adjusted for age, sex, and comorbidity.

sistant; none of these strains were associated with adverse health effects. Within 30 days of the date of receipt of samples, the patients infected with a campylobacter isolate resistant to quinolone only had a 4.48 times (95% confidence interval [CI], 1.23–16.30 times) higher risk of invasive illness or death than did the patients infected with a quinolone- and erythromycin-susceptible isolate (table 1). This result is in the same range as that obtained when the DANMAP 27-mm breakpoint was used.

Macrolides bind irreversibly to the bacterial ribosome, which results in inhibition of protein synthesis. Chromosomal mutations in the gene encoding 23S rRNA are often responsible for erythromycin resistance [3]. These mutations result in substantial changes in erythromycin susceptibility, and, as is the case for quinolones, erythromycin-resistant and -susceptible isolates represent distinct populations of bacteria. As we did for quinolones, we reanalyzed our data in a model in which only isolates with an inhibition zone $\leqslant$20 mm (the CLSI breakpoint) were considered to be resistant to erythromycin, not those with an inhibition zone <27 mm (the DANMAP breakpoint). This resulted in reclassifying 77 (2.2%) isolates as susceptible; there were no isolates from patients with adverse health events in this group. Within 90 days of the date of receipt of samples, the patients infected with an erythromycin-resistant campylobacter strain had an 8.60 times (95% CI, 1.86–39.77 times) higher risk of invasive illness or death than did the patients infected with a quinolone- and erythromycin-susceptible strain (table 1).

In conclusion, we thank Shryock for his letter [7] and his interest in our work. We agree that it is important to use internationally recognized susceptibility standards, such as those of the CLSI. However, the classification of isolates was robust to the choice of breakpoints, because the conclusions of our study were not modified by a change from the DANMAP breakpoints to the Rosco recommendations for zone diameter interpretative criteria according to CLSI recommendations.

Acknowledgments

We thank Dominique L. Monnet and Jørgen H. Engberg (Statens Serum Institut) and Frank Aarestrup (Danish Institute for Food and Veterinary Research), for reviewing this letter.

Morten Helms, Jacob B. Simonsen, Katharina E. P. Olsen, and Kåre Mølbak

Statens Serum Institut, Copenhagen, Denmark

References

1. Gootz TD, Martin BA. Characterization of high-level quinolone resistance in *Campylobacter jejuni*. Antimicrob Agents Chemother **1991**; 35:840–45.
2. Taylor DE, Ng LK, Lior H. Susceptibility of *Campylobacter* species to nalidixic acid, enoxacin, and other DNA gyrase inhibitors. Antimicrob Agents Chemother **1985**; 28:708–10.
3. Engberg J, Aarestrup FM, Taylor DE, Gerner-Smidt P, Nachamkin I. Quinolone and macrolide resistance in *Campylobacter jejuni* and *C. coli:* resistance mechanisms and trends in human isolates. Emerg Infect Dis **2001**; 7:24–34.
4. Danish Integrated Antimicrobial Resistance and Monitoring and Research Programme. DANMAP 99: consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark [ISSN 1600-2032]. Available at: http://www.dfvf.dk/Files/Filer/Zoonosecentret/Publikationer/Danmap/Danmap_1999.pdf. Accessed 15 May 2005.
5. Nachamkin I, Engberg J, Aarestrup FM. Diagnosis and antimicrobial susceptibility of *Campylobacter* species. In: Nachamkin I, Blaser MJ, eds. *Campylobacter.* 2nd ed. Washington, DC: ASM Press, **2000**:45–66.
6. Rosco Diagnostica A/S. Neo-Sensitabs™ User's Guide. 17th ed. **2004**. Available at: http://www.rosco.dk/Default.asp?ID=198. Accessed 15 May 2005.
7. Shryock TR. Internationally recognized antimicrobial susceptibility testing methods and interpretive criteria: the case for conformity (letter). J Infect Dis **2005**; 192:2027–8 (in this issue).

Potential conflicts of interest: none reported.

Reprints or correspondence: Dr. Morten Helms, Statens Serum Institut, Artillerivej 5, Copenhagen 2300 S, Denmark (mhe@ssi.dk).

The Journal of Infectious Diseases 2005; 192:2028–9

Salmonella Serotype Typhimurium, Not Antimicrobial Resistance Per Se, Is Associated with Excess Bloodstream Infections and Hospitalizations

To the Editor—Varma et al. [1] recently conducted a study to determine whether infections caused by antimicrobial-resistant nontyphoidal *Salmonella* strains are more likely than infections caused by susceptible strains to result in bloodstream infection and hospitalization. They concluded that this is, indeed, the case and that mitigation of antimicrobial resistance in *Salmonella* is likely to benefit human health. However, we believe that these important conclusions are not justified by the data and analyses presented.

First, it is not clear that the hypothesized causal chain from resistance to bloodstream invasion to hospitalization favored by Varma et al. provides a correct interpretation of the data. An alternative hypothesis is that bloodstream invasion (perhaps associated with an underlying predisposition in hospitalized patients, as Varma et al. note) leads to increased resistance as a consequence of therapy and then to adverse health consequences, including spread among patients, as is known to occur with salmonellosis among very young patients and elderly patients in hospitals and similar institutions. Similarly, excess morbidity and mortality might be expected in patients with long and/or repeated hospitalization, independent of resistance. In this case, contrary to Varma et al.'s main conclusion, mitigating resistance may have little or no impact on reducing these adverse health outcomes, which are *associated* with hospitalization (and, hence, with resistance) but are *caused* by severe underlying illnesses. Unfortunately, the data reported by Varma et al. do not indicate which model is correct, because they do not include the reasons for the patients being admitted to the hospital, where their salmonella infection was acquired,

or at what stage resistance was acquired, nor do we know whether there are, indeed, any excess adverse consequences.

Second, Varma et al. do not discuss which specific serotypes are involved in resistant infection. However, we calculate, on the basis of other National Antimicrobial Resistance Monitoring System data (available at: http://www.cdc.gov/narms/annual/2000/tables/table_8.htm), that it is probable that most of the resistant strains were, in fact, *Salmonella* serotype Typhimurium. Among several thousand nontyphoidal salmonella isolates examined in 2000, 56% of those resistant to >1 antibiotic—and 80% of those resistant to >5 antibiotics—belonged to the Typhimurium serotype. Varma et al. state that the association among resistance, bloodstream infection, and hospitalization was particularly strong for patients infected with *Salmonella* Typhimurium, but they provide no clear factual support for this or for their belief that this association is not fully explained by the fact that all 3 events are associated with *Salmonella* Typhimurium. Although a database including only 56 ascertained hospitalized patients (their table 4) with bloodstream salmonella infection is admittedly limited, we believe that what Varma et al. have probably shown is no more than that antimicrobial-resistant and possibly more virulent *Salmonella* Typhimurium is associated with excess bloodstream infections and hospitalizations for nontyphoidal salmonella infection. Thus, more-general conclusions that "policies that reduce the antimicrobial resistance of *Salmonella*" (p. 561) are likely to have significant human health benefits or to help effectively control pandemic infection caused by related multidrug-resistant clones of this serotype do not appear to be warranted. To the contrary, a more sound understanding of the causal relationship among statistically associated outcomes is essential to the development of intervention strategies that have a high probability of being effective in producing intended results.

Louis Anthony Cox, Jr.,[1] and Ian Phillips[2]

[1]University of Colorado Health Sciences Center, Denver; [2]Medical School of Guy's and St. Thomas' Hospitals, University of London, London, United Kingdom

Reference

1. Varma JK, Mølbak K, Barrett TJ, et al. Antimicrobial-resistant nontyphoidal *Salmonella* is associated with excess bloodstream infections and hospitalizations. J Infect Dis **2005**; 191: 554–61.

Potential conflicts of interest: L.A.C. has been a paid consultant for the US Food and Drug Administration's Center for Veterinary Medicine, the Animal Health Institute, and Bayer HealthCare, with regard to the risk that fluoroquinolones in poultry pose to campylobacter infection in humans.

Reprints or correspondence: Dr. Louis Anthony Cox, Jr., 503 Franklin St., Denver, CO 80218 (tcoxdenver@aol.com).

The Journal of Infectious Diseases 2005; 192:2029–30
 0022-1899/2005/19211-0026$15.00

Reply to Cox and Phillips

To the Editor—In our study [1] analyzing data from 2 national surveillance systems, we found that patients with antimicrobial-resistant nontyphoidal *Salmonella* infection were more likely to have bloodstream infection and to be hospitalized than were patients with pansusceptible *Salmonella* infection. Furthermore, among patients with the most common serotype, *Salmonella* serotype Typhimurium, the association among resistance, bloodstream infection, and hospitalization was particularly strong.

Cox and Phillips [2] apparently do not dispute these findings but object to the assumption that the emergence of resistance in nontyphoidal *Salmonella* is primarily a consequence of selective pressure associated with the use of antimicrobial agents in food animals. Despite the widespread endorsement of this assumption by the scientific community [3, 4], Cox and Phillips offer an alternative hypothesis for the emergence of resistance in nontyphoidal *Salmonella*: the use of antimicrobial agents in humans. Cox and Phillips suggest that the observed association between increased antimicrobial resistance and the increased frequency of bloodstream infection is a result of patients with bloodstream infection being more likely to receive antimicrobial therapy, and this putative increased use of antimicrobial therapy results in increased resistance. In this scenario, patients are first infected with a susceptible nontyphoidal *Salmonella* strain, then treated with antimicrobial agents; the strain becomes resistant as a consequence of the antimicrobial therapy in the patients, and then the resistant strain is further transmitted nosocomially, primarily person to person.

Although events comparable to the Cox and Phillips scenario have been occasionally described as a source of resistant strains, it is a rare occurrence with nontyphoidal *Salmonella;* the emergence of resistance in *Salmonella* during treatment in humans does not occur frequently [5, 6], and nosocomial transmission of nontyphoidal *Salmonella* is rare in the United States [7]. Investigations of outbreaks have found that, when patients are infected with antimicrobial-resistant *Salmonella,* the strain of *Salmonella* is already resistant when it infects the patients. In foodborne disease–outbreak investigations involving antimicrobial-resistant nontyphoidal *Salmonella,* for example, the antimicrobial resistance patterns of *Salmonella* isolated from patients and contaminated food that caused the outbreak typically match [8].

Furthermore, because antimicrobial therapy is common for patients with *Salmonella* who seek medical attention, patients with severe (i.e., bloodstream) infection may not be more likely than other patients with laboratory-confirmed infection to receive antimicrobial therapy. In a recent case-control study of 215 patients with sporadic laboratory-confirmed *Salmonella* serotype Newport infection, for example, more than two-thirds of patients were treated with antimicrobial

agents, and patients with severe infection were not more likely than patients with less severe infection to receive antimicrobial therapy [9]. Also noteworthy in that study is that 56% of the patients who received antimicrobial therapy received fluoroquinolones, yet none of the isolates were quinolone resistant [9].

Finally, the temporal relationship between the collection of the specimen that yielded *Salmonella* and the initiation of antimicrobial therapy indicates that, when patients are infected with antimicrobial-resistant *Salmonella,* in almost all instances the strain of *Salmonella* is already resistant when it infects the patient. In the *Salmonella* Newport case-control study, of the 131 patients for whom both date of specimen collection and date of initiation of antimicrobial therapy were reported, 83% began antimicrobial therapy ⩾1 day after specimen collection, 3% began therapy on the day of specimen collection, 5% began therapy 1 day before specimen collection, and only 9% began therapy >1 day before specimen collection (Centers for Disease Control and Prevention, unpublished data).

Cox and Phillips also suggest that our findings may have been a consequence of a limited number of more virulent *Salmonella* Typhimurium strains. We controlled for *Salmonella* serotype in our multivariable analysis, however, and found an association between resistance and an increased frequency of bloodstream infection and hospitalization. These analyses indicate that, although our findings are particularly strong among Typhimurium strains, they are not limited to Typhimurium.

We agree that continued surveillance and research are needed to more fully understand the complex epidemiology of *Salmonella.* However, our findings and those of other researchers [10] provide strong evidence that antimicrobial resistance among nontyphoidal *Salmonella* is associated with increased human health consequences. We find it necessary, therefore, to reiterate our conclusion that policies that reduce the antimicrobial resistance of *Salmonella* are likely to benefit human health. Because antimicrobial resistance in nontyphoidal *Salmonella* is primarily a consequence of use of antimicrobial agents in food animals, these policies need to include a reduction in the overuse and misuse of antimicrobial agents in food animals.

Jay K. Varma,[1,2] Kåre Mølbak,[7] Timothy F. Jones,[3] Kirk E. Smith,[4] Duc J. Vugia,[5] Timothy J. Barrett,[2] Therese Rabatsky-Ehr,[6] and Frederick J. Angulo[2]

[1]Epidemic Intelligence Service, Epidemiology Program Office, and [2]Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, [3]Tennessee Department of Health, Nashville, [4]Minnesota Department of Public Health, Minneapolis, [5]California Department of Health Services, Berkeley, and [6]Connecticut Department of Public Health, Hartford; [7]Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark

References

1. Varma JK, Mølbak K, Barrett TJ, et al. Antimicrobial-resistant nontyphoidal *Salmonella* is associated with excess bloodstream infections and hospitalizations. J Infect Dis **2005**; 191: 554–61.
2. Cox LA Jr, Phillips I. *Salmonella* serotype Typhimurium, not antimicrobial resistance per se, is associated with excess bloodstream infections and hospitalizations [letter]. J Infect Dis **2005**; 192:2029–30 (in this issue).
3. Angulo FJ, Johnson KR, Tauxe RV, Cohen ML. Origins and consequences of antimicrobial-resistant nontyphoidal *Salmonella:* implications for the use of fluoroquinolones in food animals. Microb Drug Resist **2000**; 6:77–83.
4. World Health Organization. Joint FAO/OIE/WHO expert workshop on non-human antimicrobial usage and antimicrobial resistance: scientific assessment (Geneva, 1–5 December 2003). Available at: http://www.who.int/foodsafety/publications/micro/nov2003/en/. Accessed 18 October 2005.
5. Aserkoff B, Bennett JV. Effect of antibiotic therapy in acute salmonellosis on the fecal excretion of salmonellae. N Eng J Med **1969**; 281:636–40.
6. Platt DJ, Sommerville JS, Gribben J. Sequential acquisition of R-plasmids *in vivo* by *Salmonella typhimurium.* J Antimicrob Chemother **1984**; 13:65–9.
7. Olsen SJ, DeBess EE, McGivern TE, et al. A nosocomial outbreak of fluoroquinolone-resistant *Salmonella* infections. N Eng J Med **2001**; 344:1572–9.
8. Varma JK, Greene KD, Ovitt J, et al. Hospitalization and antimicrobial resistance in *Salmonella* outbreaks, 1984-2002. Emerg Infect Dis **2005**; 11:943–6.
9. Devasia RA, Varma JK, Whichard J, et al. Antimicrobial use and outcomes in patients with multidrug-resistant and pansusceptible *Salmonella* Newport infections, 2002-2003. Microb Drug Resist (in press).
10. Angulo FJ, Nargund VN, Chiller TC. Evidence of an association between use of anti-microbial agents in food animals and anti-microbial resistance among bacteria isolated from humans and the human health consequences of such resistance. J Vet Med B Infect Dis Vet Public Health **2004**; 51:374–9.

Potential conflicts of interest: none reported.

Reprints or correspondence: Dr. Frederick J. Angulo, Centers for Disease Control and Prevention, Foodborne and Diarrheal Diseases Branch, 1600 Clifton Rd. NE, MS D63, Atlanta, GA 30333 (fja0@cdc.gov).

The Journal of Infectious Diseases 2005; 192:2030–1
 0022-1899/2005/19211-0027$15.00